Moyamoya Disease in Taiwan

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Moyamoya disease occurring in Chinese has been inadequately described. Here we report 13 cases of this disease identified by review of 3,200 cerebral angiograms performed between August 1979 and March 1986. Nine were males and four were females; there were 12 adults (aged 34–51 years) and one child (aged 11 years). All had hemorrhagic strokes with one exception, a patient with an occipital infarction. Intraventricular hemorrhage was noted by computed tomography in 10; five of these emanated from the caudate nucleus. A localized hematoma without intraventricular hemorrhage was found in two. All 13 angiograms had smokelike basal anastomoses with various degrees of stenosis or occlusion of the anterior portion of the circle of Willis; the involvement was bilateral in 12 and unilateral in one. Aneurysms were found in two patients, one in the anterior communicating artery and the other in the left anterior choroidal artery. Eleven patients recovered from the initial stroke, but two died with recurrent hemorrhage. This series differs from the series reported in Japan by the predominance of adult males. The high incidence of intraventricular hemorrhage and intracerebral hematoma is not in keeping with the previous Chinese series, in which subarachnoid hemorrhage was suspected to be the major clinical manifestation. (Stroke 1988;19:53–59)

Moyamoya disease is the angiographic diagnosis of a clinical syndrome showing bilateral stenosis or occlusion of the distal internal carotid arteries (ICAs) and their major branches, with extensive parenchymal, leptomeningeal, or transdural anastomoses. The variety of names applied to this syndrome include cerebral juxtabasilar telangiectasia, cerebral basal rete mirabile, Nishimoto's disease, spontaneous occlusion of the circle of Willis, and multiple progressive intracranial arterial occlusion. The most characteristic angiographic finding is an abnormal hemangiomatous collateral network at the base of the brain that resembles a puff of cigarette smoke drifting in the air, fitting the Japanese adjective "moyamoya," which has become the popular designation of this disease. This particular type of cerebrovascular abnormality is not confined to the Japanese, and similar cases have been reported from all over the world.2-5

In the English language literature, however, there have been only four reports among Chinese: one from Hong Kong2 and three from China.6-8 This is rather surprising since the Japanese and the Chinese are ethnically similar. The previous reports of Chinese cases have the following characteristics: 1) predominant adult onset6-8 and male predominance5,8 in contrast to the Japanese series,9-12 2) high incidence of subarachnoid hemorrhage (SAH),10-13 and 3) leptospirosis cerebral arteritis as a major cause.6,7 We have encountered 13 cases of moyamoya disease after the introduction of cranial computed tomography (CT) to our hospital in August 1979. Some clinical features of our patients resemble those of the previous Chinese cases. However, leptospirosis infection was not seen in our cases, and none had a primary SAH by CCT. Here we summarize our experience with moyamoya disease among Chinese in Taiwan and compare it with that reported from Japan, Hong Kong, and mainland China.

Subjects and Methods

Between August 1979 and March 1986, 3,200 patients underwent cerebral angiography in the Chang Gung Memorial Hospital, which has an average daily census of 1,500 and is the largest private teaching hospital in Taiwan. The clinical features and angiograms of 13 patients with moyamoya disease were reviewed and analyzed.

Results

Clinical Manifestations

Table 1 summarizes the clinical data. There were nine males and four females; the age of onset ranged from 11 to 51 (mean 40) years. Only one patient (Case 6) was younger than 20 years old; all but one (Case 1) began abruptly.

Headache and vomiting with or without disturbance of consciousness were the most frequent presenting symptoms and occurred in 11 (85%), including the only child. Neck stiffness was present on admission in these 11 patients; four of these 11 (36%) had a mild hemiparesis. Before CCT, SAH due to rupture of an aneurysm or arteriovenous malformation was suspected in these 11 cases.

Of the two patients without neck stiffness, one (Case 13) presented with an acute confusional state and transient right leg weakness and was initially referred to a psychiatrist; Case 1 presented with progressive blurring of vision and memory impairment, and brain tumor was initially suspected. None of the 13 patients had a history of stroke or transient ischemic attack.

Risk Factors

Mild hypertension was present in two patients (Cases 1 and 13). In Case 1, coarctation of the aorta...
Table 1. Synopsis of Clinical Data in 13 Patients With Moyamoya Disease

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at onset (yr)</th>
<th>Sex</th>
<th>Clinical presentations</th>
<th>Risk factor</th>
<th>CCT findings</th>
<th>Special angiographic findings</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>M</td>
<td>R homonymous hemianopsia, memory impairment</td>
<td>Hypertension</td>
<td>L occipital infarct</td>
<td>Coarctation of aorta</td>
<td>Lost to FU</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>M</td>
<td>HA, vomiting, neck stiffness</td>
<td>(—)</td>
<td>Primary IVH</td>
<td>Hypoplasia of R ICA and ECA</td>
<td>Second IVH 11 months later, died</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>M</td>
<td>HA, vomiting, drowsiness, neck stiffness</td>
<td>(—)</td>
<td>L caudate hem. and IVH</td>
<td>(—)</td>
<td>L thalamic hemorrhage 2 yrs later, died</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>F</td>
<td>HA, vomiting, confusion, neck stiffness</td>
<td>(—)</td>
<td>R caudate hem. and IVH</td>
<td>(—)</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>M</td>
<td>HA, vomiting, drowsiness, neck stiffness, L hemiparesis</td>
<td>(—)</td>
<td>L caudate hem. and IVH</td>
<td>(—)</td>
<td>Recovered</td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>M</td>
<td>HA, vomiting, neck stiffness, R hemiparesis</td>
<td>(—)</td>
<td>R frontal hem. and IVH</td>
<td>Aneurysm of AComA</td>
<td>Recovered</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>F</td>
<td>HA, vomiting, drowsiness, neck stiffness</td>
<td>(—)</td>
<td>(—)</td>
<td>(—)</td>
<td>(—)</td>
</tr>
<tr>
<td>8</td>
<td>51</td>
<td>M</td>
<td>HA, vomiting, neck stiffness</td>
<td>(—)</td>
<td>Primary IVH</td>
<td>Aneurysm of L AChoA</td>
<td>Lost to FU</td>
</tr>
<tr>
<td>9</td>
<td>37</td>
<td>M</td>
<td>HA, vomiting, confusion, neck stiffness, L hemiparesis</td>
<td>(—)</td>
<td>R caudate hem. and IVH</td>
<td>Occlusion of extra-cranial L ICA</td>
<td>Recovered</td>
</tr>
<tr>
<td>10</td>
<td>51</td>
<td>F</td>
<td>HA, vomiting, neck stiffness</td>
<td>(—)</td>
<td>L caudate hem. and IVH</td>
<td>(—)</td>
<td>Recovered</td>
</tr>
<tr>
<td>11</td>
<td>31</td>
<td>M</td>
<td>HA, vomiting, neck stiffness, L hemiparesis</td>
<td>(—)</td>
<td>R caudate hem. and IVH</td>
<td>Unilateral involvement</td>
<td>Recovered</td>
</tr>
<tr>
<td>12</td>
<td>51</td>
<td>F</td>
<td>HA, drowsiness, neck stiffness</td>
<td>(—)</td>
<td>R temporal hem.</td>
<td>(—)</td>
<td>Recovered</td>
</tr>
<tr>
<td>13</td>
<td>45</td>
<td>M</td>
<td>Mental change, R leg weakness, HA</td>
<td>Hypertension</td>
<td>R frontal and caudate hem.</td>
<td>Stenosis of L CCA bifurcation</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

CCT, cranial computed tomography; M, male; F, female; R, right; L, left; FU, follow-up; HA, headache; IVH, intraventricular hemorrhage; ICA, internal carotid artery; ECA, external carotid artery; TB, tuberculosis; hem., hemorrhage; AComA, anterior communicating artery; AChoA, anterior choroidal artery; CCA, common carotid artery. (—), absent.

was visible on an arch aortogram. No other risk factors for stroke were found. Routine blood chemistry, electrocardiography, chest x-rays, complete blood counts, and VDRL were unremarkable. The erythrocyte sedimentation rate was elevated in two patients (Cases 2 and 9). Screening tests for collagen-vascular disease including antinuclear antibody, lupus erythematosus cell preparation, and rheumatoid factor were studied in three cases (Cases 2, 4, and 6), and were all negative. One patient (Case 3) had a history of pulmonary tuberculosis (TB) 14 years before; however, chest x-ray showed no active TB, and cerebrospinal fluid (CSF) study did not reveal changes of TB meningitis.

Cranial Computed Tomography Findings

All patients underwent CCT. Intraventricular hemorrhage (IVH) was found in 10 (77%). Of these 10, five bled in the head of the caudate nucleus (Figure 1), one in the right thalamus, one in the right medial frontal lobe, and one in the left medial temporal lobe; there was no evidence of parenchymal origin in two. A localized hematoma without ventricular rupture was found in two patients, one in the right temporal lobe and one in both left frontal lobe and head of the caudate nucleus. Case 1 was the only patient to have an infarct in the left occipital area.

Contrast enhancement was done in six cases; an abnormal "wormlike" enhancement in the basal ganglia (Figure 2) was noted in only two (Cases 8 and 10). However, the anterior portion of the circle of Willis was poorly visualized in all enhanced studies (Figure 2).

Electroencephalographic Findings

Electroencephalography (EEG) was performed in five cases. Diffuse slow activity was noted in three patients; focal slow waves corresponding to the clinical and CCT findings were found in two cases. In no case was the "rebuild-up" phenomenon (see "Discussion") detected after hyperventilation.

Angiographic Findings

Cerebral angiograms including bilateral carotid and at least one vertebral artery were obtained in all 13 patients. Case 1 also underwent arch aortography because of a cardiac murmur. Characteristic "smoke-like" basal anastomoses (Figure 3) with various degrees of stenosis or occlusion of the major arteries in
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FIGURE 1. Precontrast computed tomogram in Case 6 showing typical caudate hemorrhage (open arrow) with rupture into ventricle. Right side of body appears on left side of figure.

the anterior portion of the circle of Willis were found in all patients. Leptomeningeal anastomoses (Figure 3) coursing mainly between the posterior cerebral artery and the middle and/or anterior cerebral arteries (MCA and/or ACA) were present in all 13 cases, and transdural anastomoses were noted in five. The findings were bilateral except in Case 11, who had unilateral involvement with occlusion of the MCA and stenosis of the supraclinoid segment of the ICA on the right. The pathologic changes in the ICA were usually limited to the carotid siphon and supraclinoid segment. However, extracranial lesions were also noted in three patients. These included hypoplasia of the right extracranial ICA and external carotid artery (ECA) in Case 2, occlusion of the left extracranial ICA distal to the common carotid artery (CCA) bifurcation in Case 9, and stenosis of the left CCA bifurcation in Case 13. Case 2 also had a congenital anomaly with bilateral CCAs arising from a common trunk and the right ICA terminating as the ophthalmic artery (Figure 4). Aneurysms were found in two patients; one in the anterior communicating artery (Case 7) and the other in the left anterior choroidal artery (Case 8) (Figure 5).

Course and Outcome

Most patients recovered satisfactorily from the insult of the initial stroke (Table 1). However, there were

FIGURE 2. Computed tomo-
grams after contrast medium in-
jection in Case 10 showing curvi-
linear enhancement in basal gan-
glia and left parietal cortex (arrowheads). Also note poor visualization of anterior portion of circle of Willis in contrast to posterior portion.
FIGURE 3. Left (A and B) and right (C and D) carotid angiograms in Case 10 showing occlusion or marked stenosis of bilateral M1 and A1 segments with prominent basal anastomoses. Also note leptomeningeal (arrowheads) and transdural (open arrow) anastomoses.

two patients with recurrent hemorrhage who died. Case 2 suffered a second episode of massive IVH 11 months after the first attack and died despite a ventriculoperitoneal shunt operation to relieve hydrocephalus; Case 4 sustained another stroke 2 years later that was due to a right thalamic hemorrhage and died 1 year after the second episode. In all patients, no specific treatment was given. Three patients were lost to follow-up; the remaining eight were all independent in daily activity without further vascular event during a follow-up period of 7 months to 4 years.

Discussion

Moyamoya disease is a rare cerebrovascular disorder. Its incidence is higher in Japan than elsewhere, but even in Japanese the incidence is estimated to be <1 patient per 100,000 population. Though in our study there was an incidence of 0.4% in patients undergoing cerebral angiography, we do not yet know the true incidence of moyamoya disease in Chinese. Our experience in Chinese patients had several clinical differences from Japanese reports. In Japan,9-12 the age of onset in moyamoya disease was bimodal with one peak occurring in the first decade and the second in the fourth decade, whereas we had only one child among 13 patients. This rarity of the disease in children was also found in Hong Kong5 and mainland China. In Japan, there is a female preponderance,9-12 whereas our data showed a male dominance with a male: female ratio of 2.3:1, as was the case in mainland China.9 The differences in age and sex distributions between the Chinese and Japanese are summarized in Table 2.

In 11 of our 13 patients (85%), the presenting symptoms could not be distinguished from those of SAH and would have been diagnosed as SAH prior to CCT, as was the case in Hong Kong5 and mainland China,4 where a SAH syndrome was diagnosed in 82% (9 of 11 patients) and 67% (18 of 27 patients), respectively. In Japanese reports,9-12 the clinical manifestations varied with age. In those younger than 16 years old, recurrent episodes of cerebral ischemia were the most frequent manifestations, whereas adults more commonly had intracranial hemorrhages. In the two reports of Chinese,13,14 the most common manifestation was SAH, a diagnosis based solely on CSF examination. With CCT, however, none of our patients had a primary SAH; instead, IVH was the most frequent finding and was present in 10 (77%). Primary IVH was found in only two (Cases 2 and 8), and the others bled from the paraventricular areas. The high incidence of caudate...
hemorrhage (five patients) with ventricular rupture is striking. Although caudate hemorrhage has been recognized as one of the locations for hypertensive intracerebral hemorrhage and accounts for 7% of all these hemorrhages, our findings suggest that any young adult with caudate hemorrhage and without hypertension should undergo angiographic study for moyamoya disease. This is especially true for Orientals.

The value of CCT for specific diagnosis of moyamoya disease is limited. One recent report found that CCT with contrast enhancement often reveals tortuous, curvilinear vessels in the basal ganglia, and the proximal ACA and MCA are often poorly visualized. Six of our 13 patients underwent contrast-enhanced CCT. The anterior portion of the circle of Willis was poorly visualized in all six cases, and abnormal wormlike enhancement corresponding to the extensive parenchymal collaterals was noted in only two (Cases 8 and 10). CCT demonstration of these findings suggests moyamoya disease; however, the diagnosis can be ascertained only by angiography. One must be cautious regarding contrast CCT to visualize vascular abnormalities since CCT may be affected by many factors including the dose and timing of contrast medium injection, head position, slice thickness, and quality of the machine.

EEG is of little value in detecting this disease. A return of high-voltage slow waves after termination of hyperventilation has been described as a useful screening test. However, none of our five patients having EEG showed this characteristic rebuild-up phenomenon. We agree with Nishimoto and Takeuchi that EEG is of little use for diagnosis.

All 13 of our patients had the hallmark angiographic appearance of moyamoya disease. Though it commonly involves both hemispheres, unilateral involvement (e.g., Case 11) has been reported, and a review of moyamoya-like diseases in the world literature found that most cases showed unilateral involvement. Attention was also called to the associated ventricular hemorrhages. Various causes including TB meningitis, radiation, and arteriosclerosis can produce a moyamoya-like disease; however, spontaneous MCA occlusion, which has been proved in one autopsy case, is the most common cause. Our Case 11, with IVH and spontaneous occlusion of the right MCA at the age of 31 years, supports this view.

Moyamoya disease usually affects the intracranial ICAs while the extracranial ICAs, vertebrobasilar system, and ECAs appear normal. We found an abnormality of the extracranial ICA in three of our patients. In Case 2, the multiple congenital anomalies imply an
arterial dysplastic process as basic to the disease. Case 9 had occlusion of the left extracranial ICA at a site uncommon for atherosclerotic occlusion. Murphy and Handa and Handa have reported several cases with progressive narrowing of the cervical ICA and appearance of a basal vascular network in follow-up angiograms. Although we did not perform a serial study, the angiographic findings in our Case 9 may be a late manifestation of similar progressive vascular changes in moyamoya disease. The stenotic lesion in the left CCA bifurcation of Case 13 is probably atherosclerotic in origin because the patient had a history of hypertension and was older (45 years). In Case 1, there were coarctation of the aorta and hypertension. Hypertension may accelerate the atherosclerotic process; however, whether this process accounts for the moyamoya changes in our Cases 1 and 13 is not clear.

Moyamoya disease is often accompanied by intracranial aneurysms. The frequent association of intracranial aneurysms with moyamoya disease may result from the increased blood flow and hemodynamic stress in the abnormally dilated collateral vessels. It is also possible that a congenital arterial defect predisposing to aneurysmal formation is more likely in patients with intracranial vascular anomalies such as moyamoya disease. Two of our 13 patients (Cases 7 and 8) harbored an aneurysm. A close anatomic correlation of the hematomas and aneurysms is apparent in our patients. In Case 7 a medial frontal hematoma was associated with an aneurysm in the anterior communicating artery, whereas in Case 8 a primary IVH was accompanied by an aneurysm in the anterior choroidal artery. Though there is still controversy about the cause of intracranial hemorrhage and the presence of aneurysm in moyamoya disease, our findings suggest that rupture of an aneurysm may be one cause of the bleeding in this disease.

The pathogenesis of moyamoya disease remains largely unknown. A history of inflammation in the head or neck region has been implicated; however, the specific cause is unclear. The table below provides a comparison of sex and age distributions in moyamoya disease across different studies:

<table>
<thead>
<tr>
<th></th>
<th>Japanese</th>
<th>Hong Kong</th>
<th>China</th>
<th>Taiwan</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex M:F</strong></td>
<td>45:66 (0.68)</td>
<td>5:6 (0.83)</td>
<td>20:7 (2.86)</td>
<td>9:4 (2.25)</td>
<td>34:17 (2.00)</td>
</tr>
<tr>
<td><strong>Age&gt;20 yr (%)</strong></td>
<td>32/111 (29%)</td>
<td>11/11 (100%)</td>
<td>21/27 (78%)</td>
<td>12/13 (92%)</td>
<td>44/51 (86%)</td>
</tr>
</tbody>
</table>
the history of such events is often subjective and unreliable. Tuberculous meningitis, 23 atherosclerosis, 24 neurofibromatosis, 25 and irradiation 26 have all been reported to cause this disease; a congenital cause has also been suggested. 27–29 In mainland China, leptospirosis was reported to be a major cause of the moyamoya phenomenon. 6 Leptospirosis is very rare in Taiwan. We did not perform culture or serologic tests for this organism because none of our patients had the meningitis, hepatitis, or nephritis characteristic of leptospirosis. In our series, a congenital factor is suspected in Case 2 and acquired causes in Cases 1 and 13 though we realize even these are speculative. Moyamoya disease is usually not fatal. Neurologic deficits may improve or stabilize; recurrent vascular events are common especially in children. 9–12 All 13 patients in our series recovered from the first event, but recurrence with fatal outcome occurred in two. The treatment for moyamoya disease is mainly supportive. Surgical procedures 12,13,30 such as arterial bypass, encephalomyosynangiosis, omentum transplantation, and stellate ganglionectomy have not been firmly established and are currently under investigation.

In summary, moyamoya disease is relatively uncommon among Chinese in Taiwan. The predominance of adult males is distinctly different from the Japanese experience but resembles that in Hong Kong and mainland China. IVH with or without a parenchymal origin is the most common clinical manifestation and was often diagnosed as SAH before CCT. In young adults with paraventricular hemorrhage, moyamoya disease as a cause of bleeding should always be included in the differential diagnosis. We believe that cerebral angiography for diagnosis is warranted in these patients. Aneurysms are frequently associated with this disease and are one of the causes of hemorrhage. Though most patients recover after the initial stroke, there may be recurrence and this had a poor prognosis in our series.

References

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